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Case Report

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Clinical Expression of Nickel Contact Dermatitis Primed by Diagnostic Patch Test

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Key Words
Contact dermatitis flare-up · Patch test · Nickel allergy

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Introduction

Delayed-type hypersensitivity is mediated by the immune system. Following initial allergen contact, sensitization develops and may lead to allergic contact dermatitis upon repeated allergen exposure. Clinically, erythema, swelling, blistering, itching and weeping at the site of contact develop, and spreading to uninvolved sites may occur during prolonged exposure to the eliciting antigen. Nickel is the most common allergen eliciting delayed-type hypersensitivity contact dermatitis. Nickel allergy affects people of all ages with female predominance most likely due to increased nickel contact in women via nickel-containing items. Jewelry is assumed to account for the observed female predilection.

In delayed-type hypersensitivity, prolonged allergen persistence as well as persistence of immunocompetent cells at skin sites of healed contact dermatitis have been demonstrated [1]. Postoccupational dermatitis in work-related allergic contact dermatitis is thought to be caused by allergen persistence (e.g. allergic dermatitis to chromate in masons) [2] as well as by epitope spreading to autoantigens. These factors are postulated to continue driving inflammation of the skin in spite of strict avoidance of the causative allergen.

Patch testing is used to identify allergens responsible for delayed-type hypersensitivity. Standard and suspected allergens are applied for 48 h under occlusion using Finn chambers on an uninvolved skin site such as the back. In delayed-type hypersensitivity, dermatitis in the patch test area develops and progresses even after removal of the applied allergen, distinguishing such a reaction from the more common purely irritant skin reactions. A Swedish study analyzing allergy patch tests using electron microscopy showed maintained activity of inflammatory cells in the epidermis and dermis 15–75 days following patch testing [3]. Flare-up of delayed-type hypersensitivity dermatitis triggered by patch testing [4–6] and unspecific widespread inflammatory reactions within the patch test area (angry back) are well-known phenomena [7–10].

Case Report

A 23-year-old female patient was referred to our allergy unit for a general checkup. She reported immediate-type allergies such as seasonal rhinoconjunctivitis and allergic asthma with pollen-associated food allergies and a history of drug rash to penicillin. She had been in rheumatological care for systemic lupus erythematosus for 9 years without skin involvement.

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Fig. 1. Flare-up of previous positive nickel patch test field.

Fig. 2. Dermatitis of the earlobe after wearing nickel-containing earrings.

On initial examination, the patient complained about dermatitis following application of various gels and adhesive bandages. Patch testing was performed. A standard panel of allergens was applied. Further allergens tested comprised disinfectants, preservatives, cosmetics, unguents, creams, leather and medical drugs. A complete list of allergens tested is shown in table 1. The vehicle used for test substances (by Almirall Hermal GmbH, Reinbek, Germany) was either vaseline or water, depending on solubility, with a dilution ranging from 0.01 to 100%. Finn chambers on Scanpor (Almirall Hermal GmbH) served as chambers. Adhesive bandages were attached directly to the skin. With application on day 0, the outcome readings took place on day 2 and day 3.

Positive delayed-type hypersensitivity reactions were noted for nickel sulfate and potassium dichromate. Different types of adhesive bandages induced an irritant reaction. All other allergens tested negative (table 1). The patient had never noticed skin reactions to nickel-containing items such as jewelry, belt buckles, the inside part of pant buttons with nickel coating, brassieres or other such materials. The patient was thus considered to have a latent delayed-type nickel sensitization without clinical relevance.

Three weeks following the above-mentioned patch test, the patient wore earrings which in the past had been well tolerated. She subsequently developed dermatitis of both earlobes within hours, and dermatitis at the site of nickel patch testing within a day. Figure 1 shows a large part of the patient's back displaying the previous patch site. No other patch test fields reacted; in particular, the test field for potassium dichromate, the second allergen that had tested positive on the patch test in addition to nickel, remained unchanged. Figure 2 shows dermatitis of the earlobe observed after a short period of wearing jewelry. Although a dimethylglyoxime test, a procedure to detect nickel release, was not performed, we assume liberation of nickel by the earrings worn.

Discussion

Allergic contact dermatitis is a delayed-type hypersensitivity reaction involving a cell-mediated allergic response with two essential stages: an induction or sensitization phase, which sensitizes the immune system to an allergen, and an elicitation phase, in which an inflammatory allergic reaction is triggered. During this process, allergen-specific skin-homing lymphocytes invade the respective skin area and result, after cessation of the acute reaction, in the generation of long-lived memory cells which accelerate and aggravate later episodes of contact dermatitis. Continuing manifestation of delayed-type hypersensitivity dermatitis in spite of allergen avoidance is well known, especially in occupational dermatitis [2, 11, 12]. Defects in downregulation of the contact hypersensitivity reaction or repeated antigen stimulation are assumed to cause flare-ups or persistence of allergic contact dermatitis [1].

Flare-up reactions at previous patch test or contact allergy sites after peroral provocation with the specific antigen (mostly nickel, betalactams and gold) are well-known phenomena discussed in several studies and case reports [13–18]. However, a flare-up at previous patch test sites following cutaneous exposure has only been described in mice [19]: nickel-sensitized mice showed a flare-up reaction at one ear when the other ear had been exposed to the antigen.

To our knowledge, we report the first flare-up of a previous patch test site following cutaneous application of nickel in an individual with hitherto clinically latent nickel sensitization. The conclusion from this clinical observation is that nickel exposure for 48 h in a patch test area under occlusion is sufficient to induce overt delayed-type hypersensitivity on re-exposure with a previously tolerated antigen in a previously clinically unresponsive individual. Similar observations have been made in an English study with fragrance mix I [20]. In our case, we interpret the positive patch

Table 1. List of allergens tested and test results

Substance	Dilution, %	48 h	72 h	Substance	Dilution, %	48 h	72 h
Lanolin alcohol	30	–	–	Chlorocresol	1	–	–
p-Phenylene diamine	1	–	–	Dichlorophene	0.5	–	–
Thiuram mix	1	–	–	Phenyl mercury acetate	0.05	–	–
Neomycin sulfate	20	–	–	Chloroxylenol	1	–	–
Cobalt (II) chloride	1	irritated	irritated	Glyoxal trimer	1	–	–
Nickel (II) sulfate	5	+	+	Iodine	0.5	–	–
Benzocaine	5	–	–	Thiomersal	0.1	–	–
Colophonium	20	–	–	Imidazolidinyl urea	2	–	–
N-isopropyl-N′-phenyl-*p*-phenylene diamine	0.1	–	–	Dibromodicyanobutane/phenoxyethanol	1	–	–
Potassium dichromate	0.5	+	+	1-(3-Chloroallyl)-3,5,7-triaza-1-azonia-adamantane chloride	1	–	–
Mercapto mix	2	–	–	Triclosan	2	–	–
Epoxy resin	1	–	–	Glutaraldehyde	0.3	–	–
Balsam of Peru	25	–	–	Chlorhexidine gluconate	0.5	–	–
p-tert-Butylphenol formaldehyde resin	1	–	–	Butylhydroxytoluol	2	–	–
Paraben mix	16	–	–	Butylhydroxyanisole	2	–	–
Fragrance mix	8	–	–	Dodecyl gallate	0.3	–	–
Mercaptobenzothiazole	2	–	–	*tert*-Butyl hydrochinone	1	–	–
Mercury (II) amide chloride	1	–	–	Hexachlorophene	1	–	–
Cetyl stearyl alcohol	20	–	–	Benzoic acid	5	–	–
Zinc diethyldithiocarbamate	1	–	–	Polyethylene glycol ointment DAB8	100	–	–
White vaseline	100	–	–	Isopropyl myristate	10	–	–
Formaldehyde	1	–	–	Adeps lanae	30	–	–
Chloromethylisothiazolinone	0.01	–	–	Propylene glycol	5	–	–
Benzalkonium chloride	0.1	–	–	Trolamine (triethanolamine)	2.5	–	–
Bronopol	0.5	–	–	Amerchol L 101	50	–	–
Tixocortol pivalate	1	–	–	Sorbitan sesquioleate	20	–	–
Hydrocortisone-17-butyrate	0.1	–	–	Lanolin alcohol ointment DAB9	100	–	–
Propolis	10	–	–	Dermaplast elastic (bandage material)		–	–
Bufexamab	5	–	–	Sparablanc (bandage material)		irritated	irritated
Lyral	5	–	–	Isofix fleece (bandage material)		–	–
Sorbic acid	2	–	–	Transpore (bandage material)		irritated	irritated
Chloracetamide	0.2	–	–	Sparablanc plastic (bandage material)		–	–
Cetylpyridinium chloride	0.1	–	–	Micropore (bandage material)		–	–
Cetalkonium chloride	0.1	–	–	Fixomull fleece (bandage material)		–	–
Diazolidinyl urea	2	–	–	Mefix (bandage material)		–	–

test to nickel not as a result of active sensitization, a rare event but reported for paraphenylene diamine [21, 22], because previous exposure to nickel before patch testing has to be assumed due to the ubiquity of nickel. Rather, we assume that patch testing boosted a previously acquired, clinically silent sensitization to nickel in this individual, resulting in overt delayed-type hypersensitivity on nickel re-exposure.

Nickel contact dermatitis on the ear was followed by a distant flare-up of the nickel patch test site. We interpret this as an antigen-specific reaction: neither did any other patch test site flare up (analogous to an angry back reaction) nor did potassium dichromate in particular, the second allergen which had shown a positive patch test reaction, cause a flare-up. We speculate that nickel allergen may remain locally at the site of previous patch testing, possibly by means of antigen-presenting cells, for weeks. Antigen-specific T lymphocytes with particular homing features may have been involved, a pathway that is discussed in the case of fixed drug eruption [23, 24].

In summary, we report the first case of a previously positive patch test site flaring up following distant contact dermatitis in a previously unresponsive person. Local persistence of antigen, professional antigen-presenting cells or lymphocytes with restricted homing behavior may explain our observation.

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